Assessment of Antibiotic Efficacy in the Management of "Priority 1: Critical" Multi-Drug Resistant Gram-Negative Bacterial Infections Enlisted by WHO

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ABSTRACT

Background: The growing resistance pattern of multidrug-resistant gram-negative bacteria is increasing, making it more crucial to use antibiotics. Our study focuses on antibiotics' rational use and efficacy for gram-negative bacterial infections. aim to find the susceptibility and the resistance pattern of the gram-negative bacteria-*P. aeruginosa, K. pneumoniae, A. baumannii*, and *E. coli* (Priority 1: Critical) to the antibiotics and to assess the antibiotic efficacy. **Materials and Methods:** It is a prospective observational study performed using an antibiogram to find susceptibility and the right use of the antibiotic for Priority 1: Critical species of gram-negative bacteria. The study involved 201 people and was carried out over a period of nine months. Statistical analysis was performed with the help of JASP software. **Results:** *Escherichia coli* being the highest gram-negative causing bacterial infections have also made it very challenging to treat the infections due to its growing resistance pattern. our study showed that Cefoperazone+sulbactam and piperacillin+tazobactam are the most susceptible drugs. The highest-resistant drugs are carbapenem, meropenem, ampicillin and ertapenem. Student-paired T-test was performed for CRP, Procalcitonin and ESR; the results were statistically significant. **Conclusion:** This study interprets the growing and new pattern of MDR that has made it a very challenging aspect of the healthcare system. It emphasizes the appropriate usage of antibiotics for better infection control and good patient outcomes.

Keywords: MDR bacterial infection, Gram-negative bacterial infection, Antibiotic in MDR, JASP software.

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INTRODUCTION

Multidrug-resistant bacteria are a solicitude in the present scenario and a growing fear among the healthcare systems.[1-4] Multidrug resistance is defined as the acquired non-susceptibility to at least one agent in three or more antimicrobial categories.[5] Due to the adaptions to different resistance mechanisms by these gram-negative bacteria, there is an increase in resistance to antibiotics. Antibiotics are a boon to the present society and also an effective therapy to treat infections rationally. The mutations and development of the different resistant mechanisms in organisms make it difficult to treat infections. Some of the factors contributing to the increasing resistance among gram-negative bacteria are firstly overuse or misuse or unnecessary use of antibiotics which has led to the development of adaptive resistance mechanisms and makes it difficult to treat the infection. Secondly, a lack of responsible antibiotic stewardship and also a lack of good infection control practices in the hospital settings have made it challenging to treat the infections. World Health Organization has differentiated bacterial organisms into various categories depending on the severity of the infections they cause. "Priority 1: critical" category consists of gram-negative bacteria that cause increased infections and may lead to severe conditions, the "Priority 2: high" category is less severe compared to the Priority 1 category and the last category is "Priority 3: medium" which causes moderate infections compared to the other 2 categories. Our study mainly focuses on "Priority 1: Critical" which includes *Acinetobacter baumannii, Pseudomonas aeruginosa, Escherichia coli*, and *Klebsiella pneumoniae* which are mostly carbapenem-resistant. These gram-negative bacteria[6,7] cause significant morbidity and mortality worldwide. Several strategies have been implemented such as a structured antibiotic policy, modification of the chemical structure of the antibiotic with new mechanisms of action, novel targets that resistant bacteria are sensitive, completion of appropriate duration of antibiotic therapy, educating the prescribers on the rational use and educating patients on the better medicine compliance. Our

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main aim is to find the susceptibility and resistance pattern of the "Priority 1: Critical" to antibiotics using the antibiogram data. Secondly to assess the antibiotic efficacy of the infections caused by these gram-negative bacteria. This helps to understand the growing pattern of resistance and provides a better treatment option based on the susceptibility of antibiotics. Antibiograms are a great advantage to the present microbiological unit that give a wide range of information on the organisms and different susceptibility and resistant patterns of the antibiotics for the inspected organism, Minimum Inhibitory Concentration (MIC) is very critical and antibiotics having lower MIC have a much greater Minimum Bactericidal Concentration (MBC) and is more effective against the organism, which makes it much easier to select an antibiotic regimen and treat the infections caused by these organisms and thereby decreasing the morbidity and mortality rates. In the epoch of antibiotic misuse, growing resistance and reduced attention to antibiotic stewardship, the need for reliable, accurate antibiogram data gives a better basis for appropriate antibiotic selection.

MATERIALS AND METHODS

Study design

A prospective and Observational study was conducted in the inpatient department of General Medicine and Infectious Diseases, using an antibiogram to find susceptibility and the right antibiotic use for specific species of gram-negative bacteria.

Data collection

A prospective and Observational study was conducted in the inpatient department of General Medicine and Infectious Diseases. The patients who met the inclusion criteria were enrolled in the study. The first step is collecting baseline information such as demographic details like age, sex, date of admission, microbiological data, antibiogram, date of onset of the treatment and date of discontinuation of the treatment. Following this, all the cultures of the samples taken from the patient, antibiotic sensitivity testing details, antibiotics that are administered based on sensitivity results, duration of the therapy, any switch of antibiotics done and symptomatic improvement in the patients were been collected and documented in a suitable data collection form. The treatment chart was followed daily and the progress reports were recorded.

Methods

A prospective and Observational study was conducted in the inpatient department of General Medicine and Infectious Diseases. Inclusion criteria for this study encompassed patients diagnosed with infections caused by Priority 1: critical multidrug-resistant gram-negative organisms including *Acinetobacter baumannii*,[7-9] *Pseudomonas aeruginosa*,[10] *Klebsiella pneumoniae* and *Escherichia coli*. Patients with comorbidities, of both genders and across all age groups were eligible for inclusion. Conversely, exclusion criteria comprised pregnant or lactating women, patients with cancer and individuals diagnosed with HIV. These criteria were employed to ensure a focused study population while excluding groups that may introduce confounding variables or require specialized considerations in treatment protocols.

The study procedure involves collecting the patient's demographic details. The empirical antibiotic data is collected after the bacterial infection is suspected for which the antibiotics are prescribed. The antibiogram contains information on the organisms that were confirmed to be present in the clinical samples, including *P. aeruginosa, K. pneumoniae, A. baumannii,* and *E. coli* isolates from sputum, urine, wound swabs, pus aspirates and vaginal swabs. The antibiogram is a critical step in making an appropriate choice of antibiotics. The empirical antibiotic data collected is been correlated to the antibiogram to assess its susceptibility, if it is susceptible to the specific species of bacteria then days of antibiotic therapy were observed. Data on the Switching of antibiotics is collected when the empirical antibiotic is switched to a better susceptible antibiotic based on the sensitivity profile. The efficacy of the antibiotic is assessed on the patient's symptomatic improvement and the laboratory data and days of the antibiotic regimen are analyzed to exhibit better infection control and good patient outcome.

Statistical Analysis

Statistical analysis was performed for the laboratory data of CRP, Procalcitonin and ESR, the values of those as mentioned earlier were taken from the patients consisting of the gram-negative bacterial infection at the time of admission and at the time of discharge. Before going for analysis, the normality of the values obtained was verified with the Shapiro-Wilk test. The Shapiro-Wilk test confirmed that the values were normally distributed. On confirmation with the normal distribution pattern, the Paired Student T-Test was performed with a 95% confidence interval (p=0.05) using the JASP Statistical Software. All the results obtained were statistically significant.

RESULTS

Demographic data

The results indicated that, of the 201 subjects, the middle age (45-59 years) category had the highest percentage of males (46%) and females (51%) who participated in the study, while the young adults (18-25 years) category had 7% and 6% of subjects in male and female respectively, which was relatively lower than other categories (Figure 1).

Organism distribution

Escherichia coli (53%) had caused the highest number of infections in patients then followed by *Klebsiella pneumoniae*

Table 1: distribution of organisms isolated from clinical specimens.

Specimens	*Pseudomonas aeruginosa* % (n)	*Klebsiella pneumoniae* % (n)	*Acinetobacter baumannii* % (n)	*Escherichia coli* % (n)	Total % (n)
Sputum	31	65	70	4	28.8 (58)
Urine	15	28	17	74	49.7 (100)
Wound swab	50	0	13	18	17.4 (35)
Pus aspirate	4	7	0	3	3.5 (7)
Vaginal swab	0	0	0	1	0.6 (1)
Total % (n)	13 (26)	23 (46)	11 (23)	53 (106)	100 (201)

Table 2: Distribution of risk factors within the study population.

Risk factors	*Pseudomonas aeruginosa* %	*Klebsiella pneumoniae* %	*Acinetobacter baumannii* %	*Escherichia coli* %
T2DM	46	0	13	21
Recurrent UTI	11	20	13	61
Pneumonia	4	65	9	1
LRTI	27	0	35	2
COPD	4	13	26	0
BPH	4	0	0	3
Appendicitis	4	0	0	0
Age	0	2	0	1
pyelonephritis	0	0	4	3
Sex	0	0	0	1
Trauma	0	0	0	1
Surgery	0	0	0	5
Cellulitis	0	0	0	1

Table 3: Distribution of diagnosis within the study population.

Diagnosis	*Pseudomonas aeruginosa* %	*Klebsiella pneumoniae* %	*Acinetobacter baumannii* %	*Escherichia coli* %
UTI	15	28	18	74
Ulcer	4	2	0	1
Ruptured appendicitis	4	0	0	1
Pneumonia	4	6	4	1
LRTI	27	55	52	2
COPD	4	5	13	0
Diabetic foot	30	2	9	10
Cellulitis	4	0	0	4
Bedsore	4	0	4	0
Abscess	4	2	0	5
Vaginal infection	0	0	0	1
Fournier's gangrene	0	0	0	1

Table 4: **Antibiotics prescribed for each gram-negative organism in the study population.**

Antibiotics	*Pseudomonas aeruginosa* %	*Klebsiella pneumoniae* %	*Acinetobacter baumannii* %	*Escherichia coli* %
Inj. Piperacillin+tazobactam	31	42	48	45
Inj. Amikacin	30	11	0	17
Inj. Ceftriaxone	23	30	13	18
Inj. Cefoperazone+sulbactam	16	0	9	17
Tab. Azithromycin	0	13	0	2
Inj. Azithromycin	0	4	0	1
Inj. Doxycycline	0	0	30	0

Table 5: **Standard dose and adjusted dose distribution of empirical and switched antibiotics in the study population.**

Antibiotics	Empirical antibiotic		Switched antibiotic	
	Standard dose %	Adjusted dose %	Standard dose %	Adjusted dose %
Inj. Piperacillin+tazobactam	95	5	100	0
Inj. Amikacin	100	0	100	0
Inj. Ceftriaxone	89	11	100	0
Inj. Cefoperazone+sulbactam	75	25	69	31
Tab. Azithromycin	100	0	100	0
Inj. Azithromycin	100	0	100	0
Inj. Doxycycline	100	0	100	0

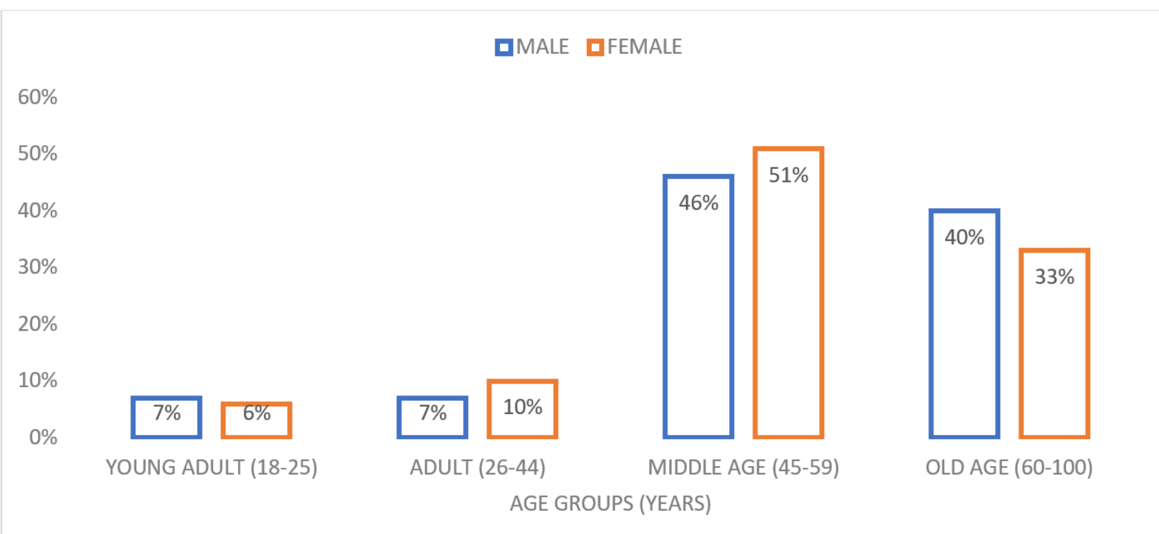

Figure 1: Age group and Gender distribution in the study population.

(23%), *Pseudomonas aeruginosa* (13%) and lastly *Acinetobacter baumannii* (11%) which is represented in Figure 2.

The microbiology data showed the highest percentage of organisms in the wound swab (50%), sputum (65%), sputum (70%) and urine (74%) of *Pseudomonas aeruginosa, Klebsiella pneumoniae, Acinetobacter baumannii* and *Escherichia coli* respectively which is depicted in Table 1.

The Table 2 interprets the risk factor distribution among 201 subjects, leading to the infection among them T2DM (46%) in *Pseudomonas aeruginosa, pneumonia* (65%) in *Klebsiella pneumoniae*, LRTI (35%) in *Acinetobacter baumannii* and recurrent UTI (61%) in *Escherichia coli* were observed to be the highest leading cause. Gender (1%), trauma (1%), surgery (5%) and cellulitis (1%) in *Escherichia coli* show the least cause for risk factors.

Diagnosis rates for diabetic foot (30%) in *Pseudomonas aeruginosa*, LRTI (55%) in *Klebsiella pneumoniae*, LRTI (52%) in *Acinetobacter baumannii* and UTI (74%) in *Escherichia coli*, were the highest. Among all the various diagnoses, vaginal infections (1%) and Fournier's gangrene (1%) were the least common infections which are depicted in Table 3.

Prescribing pattern

Antibiotics used to treat MDR-resistant gram-negative bacterial infections are shown in Figure 3. The most commonly prescribed antibiotic was Inj. Piperacillin+tazobactam (43%) followed by Inj. Ceftriaxone (21%), Inj. Amikacin (15%), Inj. Cefoperazone+sulbactam (12%), Tab. Azithromycin (4%), Inj. Doxycycline (3%) and Inj. Azithromycin (2%).

The most frequently used antibiotics among the rest were Inj. Piperacillin+tazobactam; Inj. Ceftriaxone was the second most commonly used antibiotic, followed by Inj. Amikacin and Inj. Cefaperazone+sulbactam and least used were Inj. Azithromycin, Tab. Azithromycin and Inj. Doxycycline is shown in Table 4.

Figure 4 depicts the switching of antibiotics based on the susceptibility pattern. The standard dose and adjusted dose distribution of empirical and switched antibiotics are shown in Table 5. At the onset of empirical therapy, the standard dose of the drugs was prescribed in Inj. Amikacin (100%), Tab. Azithromycin (100%), Inj. Azithromycin (100%) and Inj. Doxycycline (100%). Of the switched antibiotics, the dose adjustment was made only in Inj. Cefoperazone+sulbactam (31%).

Seven days was the longest period of antibiotic medication observed in the study population; ten days was the next highest and fourteen days was the shortest, as shown in Figure 5.

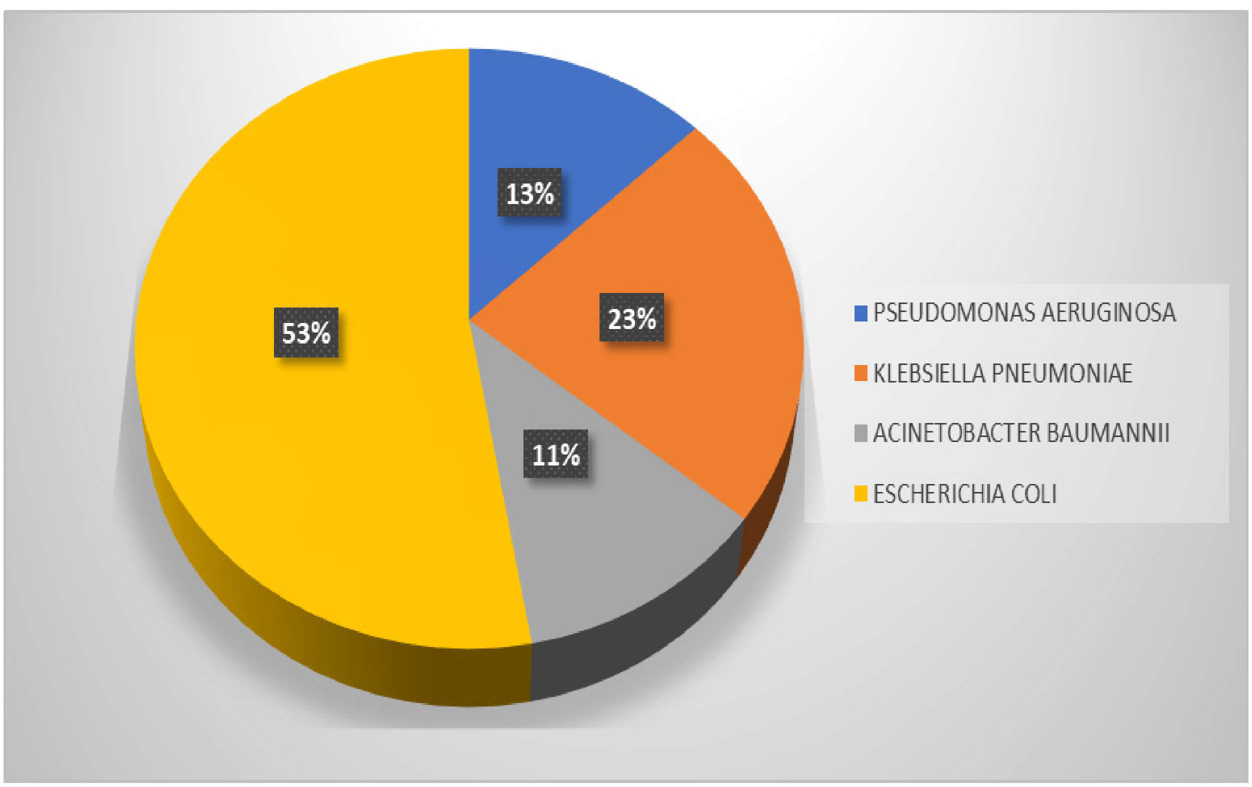

Figure 2: Percentage of organism distribution in subjects with gram-negative bacterial infections.

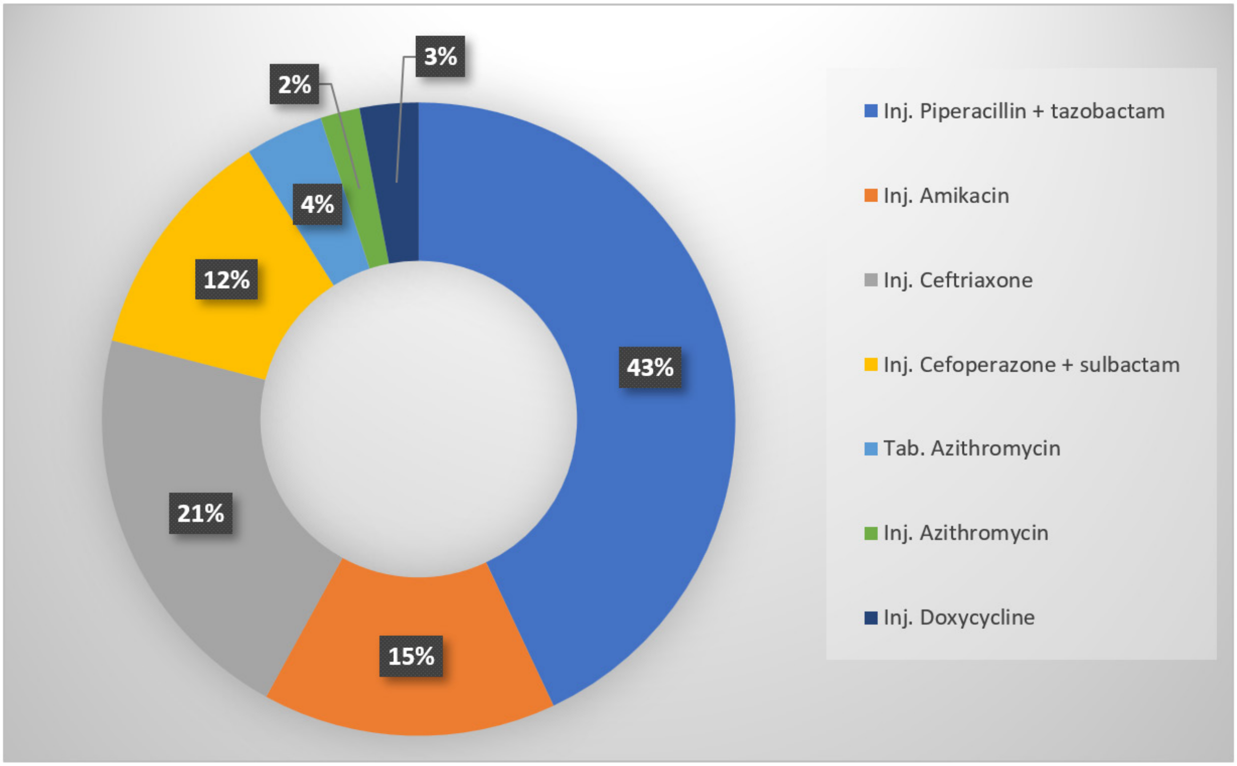

Figure 3: Antibiotic prescribed to treat gram-negative infection in the study population.

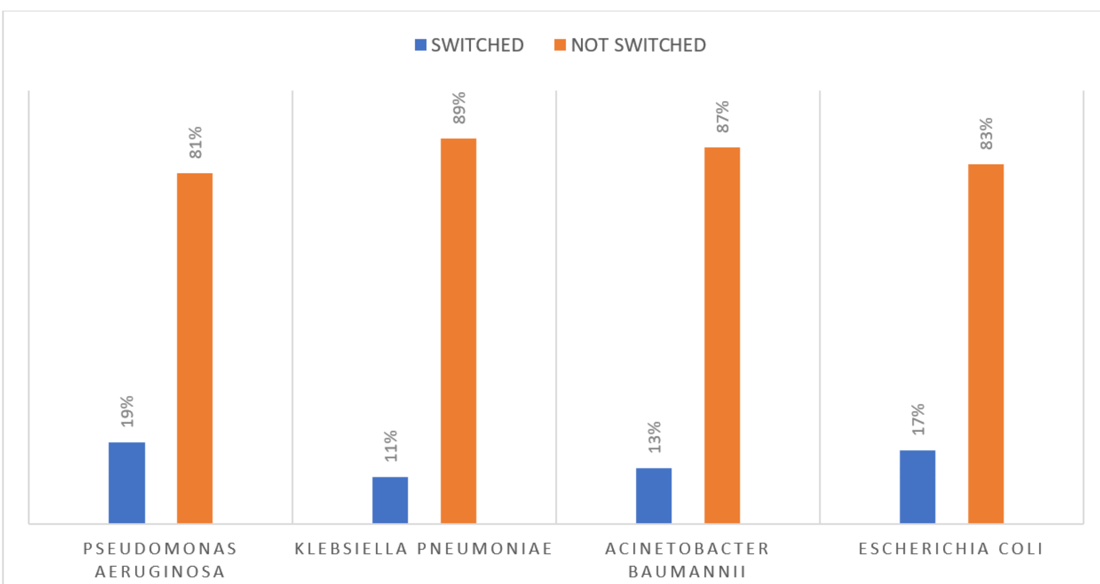

Figure 4: Switching of antibiotics based on the susceptibility pattern.

Figure 5: Days of antibiotic therapy in the study population.

Table 6a: T-test of C-reactive protein, procalcitonin and ESR distribution in the study population.

Parameters	Mean	Standard deviation	*p*-value
Pseudomonas aeruginosa			
CRP (mg/L)-first value	132.0273	±34.775	<0.00001
CRP (mg/L)-last value	3.6259	±0.501	
Procalcitonin (ng/mL) - first value	36.1303	±21.727	= 0.001818
Procalcitonin (ng/mL)-last value	0.05667	±0.0106	
ESR (mm/hr)-first value	29.6667	±0.653	<0.00001
ESR (mm/hr)-last value	7.3333	±1.307	
Klebsiella pneumoniae			
CRP (mg/L)-first value	125.0595	±28.894	<0.00001
CRP (mg/L)-last value	4.1282	±0.807	
Procalcitonin (ng/mL)-first value	36.8964	±17.267	=0.000048
Procalcitonin (ng/mL)-last value	0.159	±0.192	
ESR (mm/hr)-first value	72.6667	±36.013	=0.005014
ESR (mm/hr)-last value	8.3333	±0.653	

Efficacy outcomes

Table 6 represents the statistical analysis of paired T-test for C-reactive protein, procalcitonin and erythrocyte sedimentation rate results that were collected prior to the antibiotic therapy and at the discharge time. It showed a significant decrease in the infection from the first to the last values in all the organisms and the *p*-values obtained were statistically significant.

On the other hand, the susceptibility and resistant pattern of the antibiotic in different organisms were illustrated in Figures 6 (a-d).

DISCUSSION

Gram-negative bacterial infections are the most concerning situation in healthcare systems and a growing fear of treating them rationally as there have been no new antibiotics for 3 decades

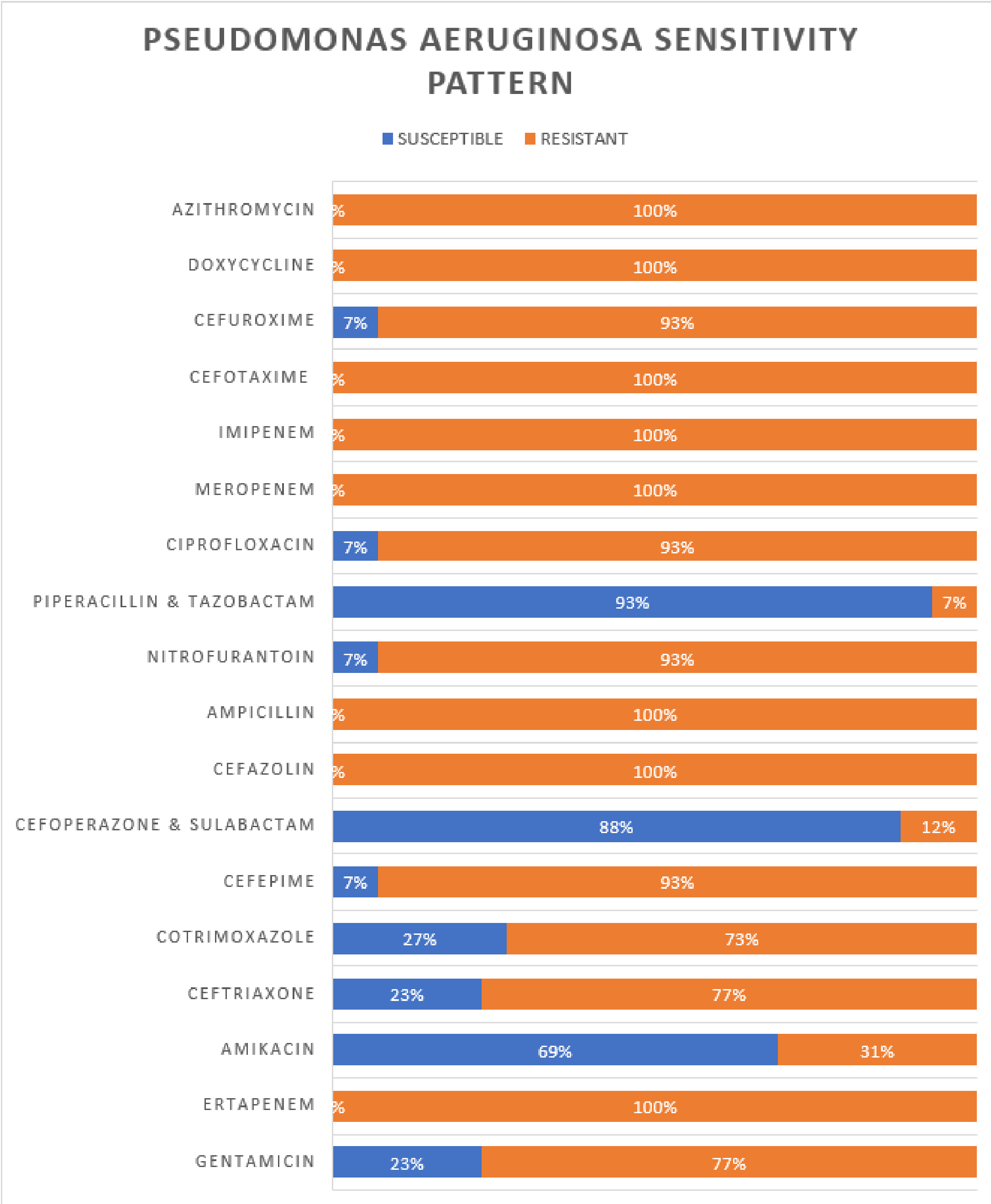

Figure 6 a: Susceptibility and resistance pattern of the antibiotics in the study population.

which is a huge challenge to face as the existing antibiotics are becoming less effective due to the growing bacterial resistance. Antibiotics are used unnecessarily and misuse of antibiotics or wrong use of antibiotics leads to exacerbation of antibiotics and thereby leading to resistance. Using the right susceptible antibiotic for the right infection with the right dose and duration of treatment can prevent the adaptive resistance caused by gram-negative bacteria.

The present study interprets the demographic data of 201 participants which emphasizes that 63% of the participants were male and 37% of the participants were female. The results show that the most infections were found in the 45 to 59 ages categories. In the organism distribution, the current study shows that the gram-negative bacterial infections were seen highest in *Escherichia coli* (53%), followed by *Klebsiella pneumoniae* (23%), *Pseudomonas aeruginosa* (13%) and lastly *Acinetobacter baumannii* (11%) which were compared with the study conducted by V.S. Doetale *et al.*[11] which showed *Escherichia coli* (53.1%), *Acinetobacter baumannii* (45.5%), *Klebsiella pneumoniae* (24.2%) and *Pseudomonas aeruginosa* (15.2%) which had caused gram-negative bacterial infections. The distribution of isolates from the clinical specimens collected in the current study shows as follows, sputum (58%), urine (49.7%), wound swab (17.4%),

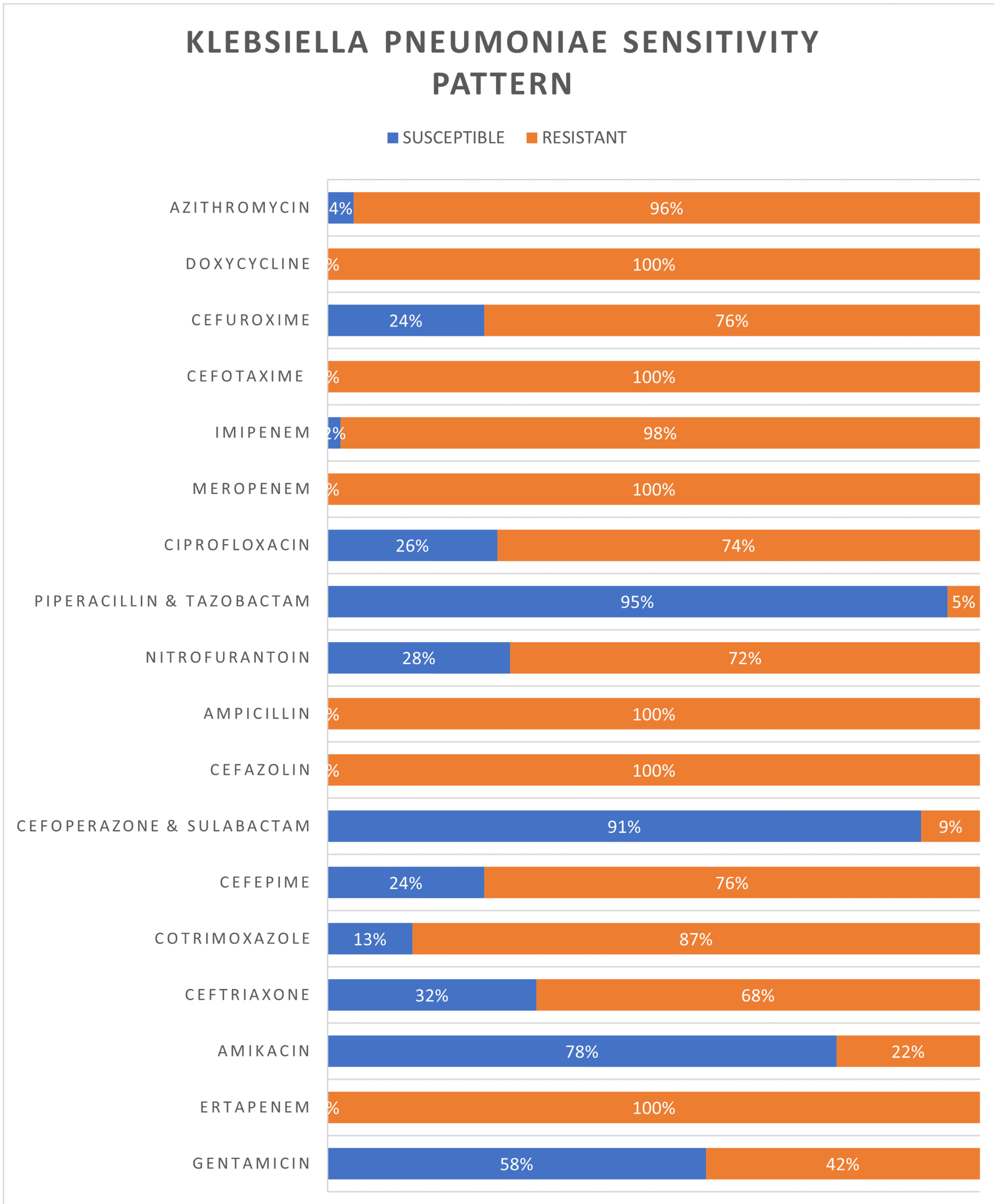

Figure 6 b: Susceptibility and resistance pattern of the antibiotics in the study population.

pus aspirate (3.5%), vaginal swab (0.6%) which was compared to the study conducted by Satyajeet K Pawar *et al.*[12] which the results were interpreted, where pus (40.5%), urine (19.2%), ETT (15.5%), body fluids (3.3%), blood (3.3%), stool (2.4%), sputum (11.7%) and other samples (4.6%), this study had various collection of specimens, as the total samples collection was done form 772 participants and provided a good result profile with the better analysis. Looking into the risk factor that has led to the development of infections among the participants, it deciphers that T2DM (46%) in *Pseudomonas aeruginosa, pneumonia*

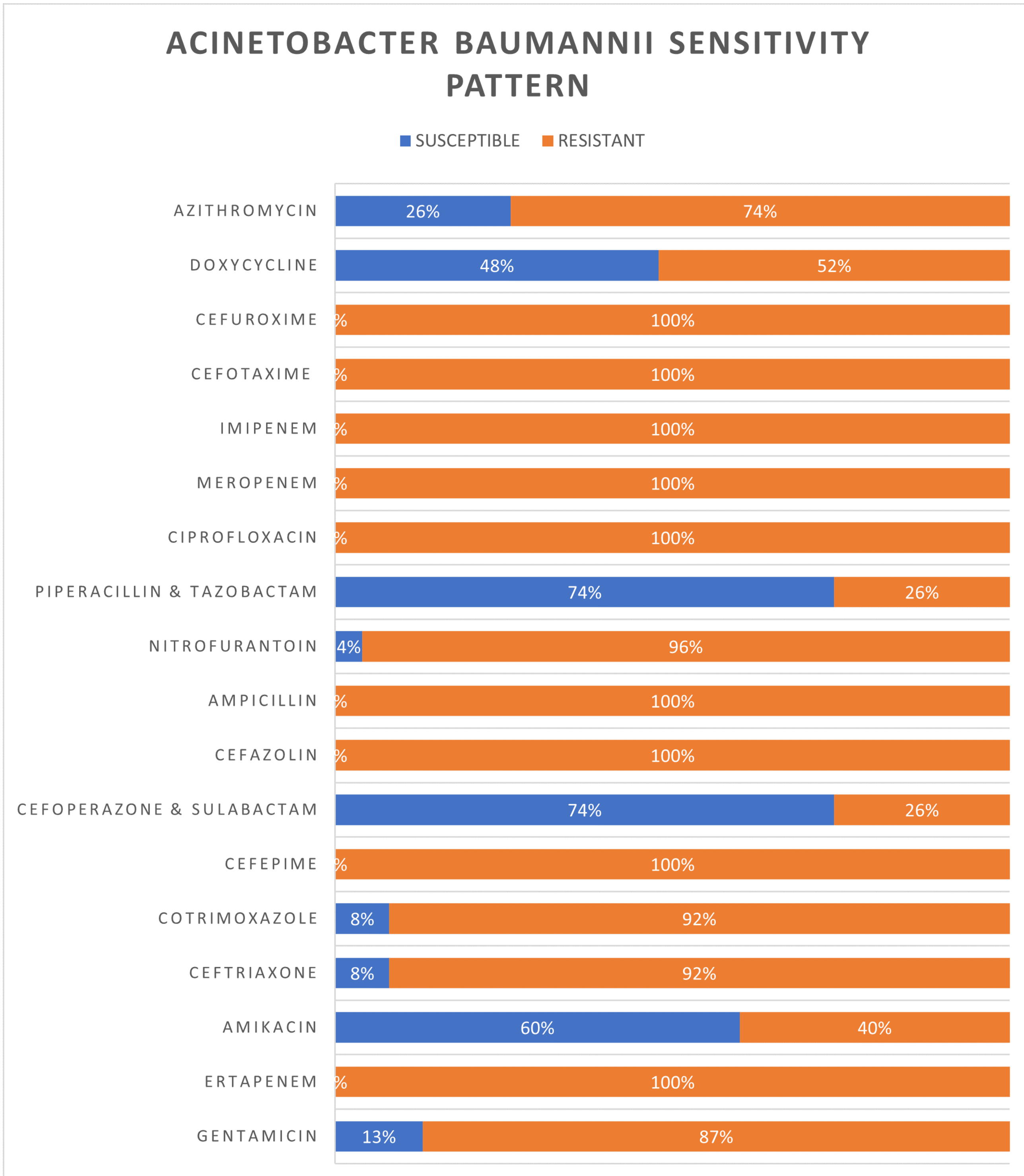

Figure 6 c: Susceptibility and resistance pattern of the antibiotics in the study population.

(65%) in *Klebsiella pneumoniae*, LRTI (35%) in *Acinetobacter baumannii* and recurrent UTI (61%) in *Escherichia coli* are the highest leading causes compared to the other risk factors.

The duration of the treatment is very important in infection prevention and also focuses on unnecessary or inappropriate use of antibiotics. In the current study, it was seen that 7 days of antibiotic therapy was efficacious in treating gram-negative bacterial infections, but only in some cases was there prolonged hospitalization for 14 days. The prescribing of antibiotics was done on the sensitivity pattern which exhibits that the Injection of Piperacillin and tazobactam and the Injection of Cefoperazone and sulbactam had better susceptibility for all 4 species of gram-negative bacteria compared to the other antibiotics. The penicillins and beta-lactamase inhibitors accounted for 42% and

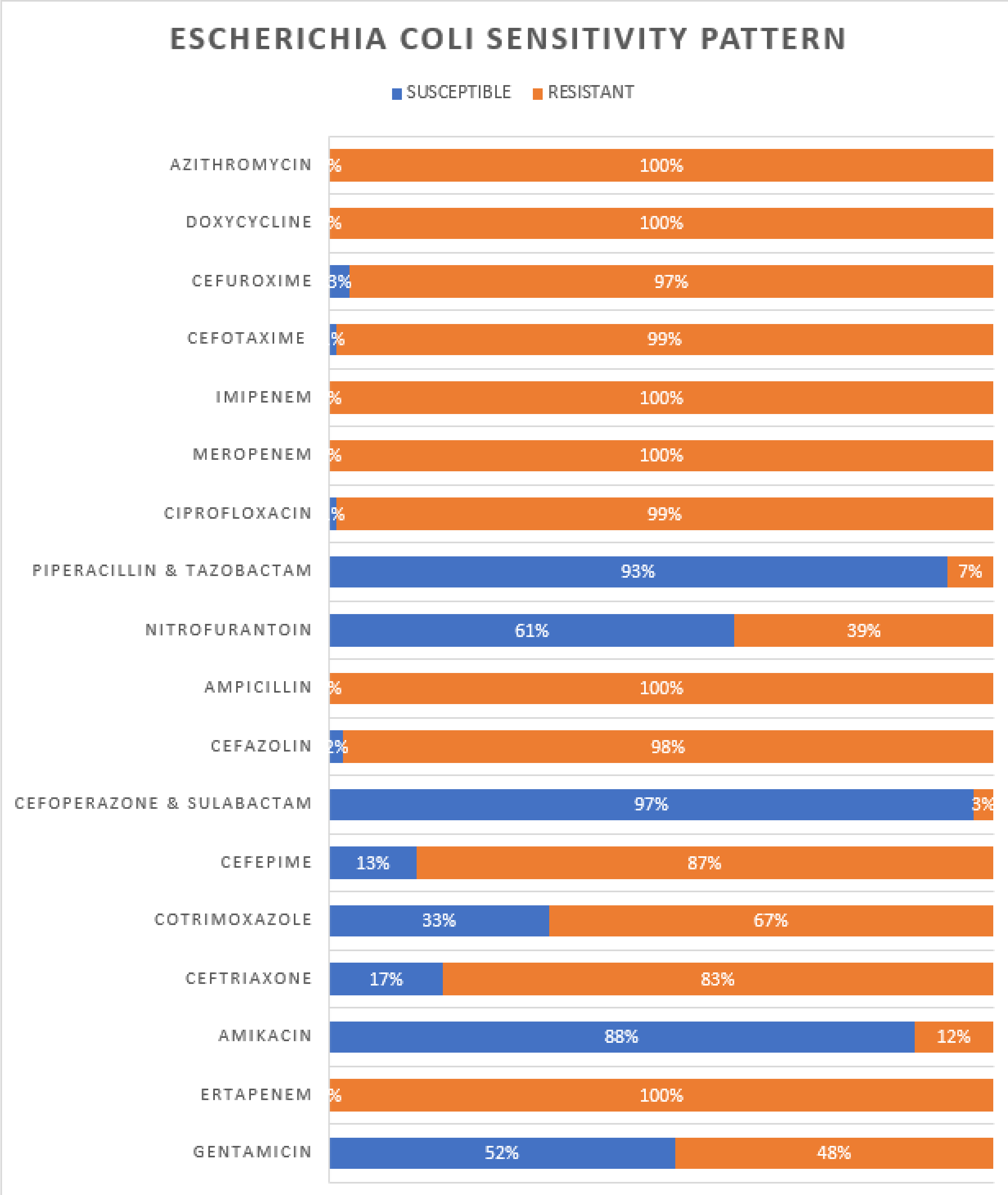

Figure 6 d: Susceptibility and resistance pattern of the antibiotics in the study population.

cephalosporins accounted for 21% among 6 different drug classes and has been proved by the current study that they are effective against gram-negative bacterial infections with better outcomes and quality of life. It is compared with the study conducted by Satyajeet K. Pawar *et al.*,[12] which emphasized that cephalosporins were the highest and accounted for 11% and the lowest accounted for 8.5% i.e. penicillin. Switching of antibiotics was done according to the sensitivity pattern.

Statistical analysis was performed for the laboratory data of CRP, Procalcitonin and ESR, the values of the above-mentioned were taken from the patients who were confirmed with gram-negative bacterial infection. All the results obtained were statistically significant and also interpreted that selecting the right susceptible

Table 6b: T-test of C-reactive protein, procalcitonin and ESR distribution in the study population.

Parameters	Mean	Standard deviation	*p*-value
Acinetobacter baumannii			
CRP (mg/L)-first value	115.5286	±33.201	<0.00001
CRP (mg/L)-last value	3.5857	±0.629	
Procalcitonin (ng/mL)-first value	46.1033	±22.718	=0.000148
Procalcitonin (ng/mL)-last value	0.06238	±0.00774	
ESR (mm/hr)-first value	110	±19.6	=0.004528
ESR (mm/hr)-last value	5.5	±0.98	
Escherichia coli			
CRP (mg/L)-first value	138.8651	±21.987	<0.00001
CRP (mg/L)-last value	3.8628	±0.43	
Procalcitonin (ng/mL)-first value	36.7687	±10.195	<0.00001
Procalcitonin (ng/mL)-last value	0.09462	±0.0529	
ESR (mm/hr)-first value	73.0714	±16.83	<0.00001
ESR (mm/hr)-last value	7.9286	±0.808	

antibiotic and treatment for the right duration of time had significantly decreased the infection and bacterial growth. There was a significant difference between the first value and the last value which was self-explanatory and achieved a better outcome in decreasing the multidrug resistant gram-negative bacterial infections.[13]

CONCLUSION

Antibiotics have been on the verge of extinct as there have been no new antibiotics past 3 decades and the growing adaptive resistance among organisms towards antibiotics has made the healthcare systems preposterous in treating the multi-drug resistance gram-negative bacteria. Rational use of antibiotics comes with precise culture reports and antibiogram consisting of sensitivity patterns, which have to be priorly tested before starting an antibiotic regimen, this helps in the rational use of antibiotics and prevents the unnecessary pill burden on the patient. Blood tests have to be evaluated before starting and after completing the antibiotic regimen to assess the gram-negative bacterial infection severity, the main marker for a precise indication of the bacterial infections is procalcitonin among the other markers. Choosing the right susceptible antibiotic with the correct duration of treatment provides a positive outcome.

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ETHICS APPROVAL

Ethical approval is not required because it is an observational study and did not administer any medicine or change any treatment plan during the study.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

***P. aeruginosa*:** *Pseudomonas aeruginosa*; ***K. pneumoniae*:** *Klebsiella pneumoniae;* ***A. baumannii*:** *Acinetobacter baumannii;* ***E. coli*:** *Escherichia coli;* **T2DM:** Type 2 Diabetes Mellitus; **LRTI:** Lower respiratory tract infection; **UTI:** Urinary Tract Infection; **CRP:** Ceactive protein; **ESR:** Erythrocyte Sedimentation Rate; **COPD:** Chronic Obstructive Pulmonary Disease; **BPH:** Benign Prostatic Hyperplasia; **MDR:** Multi-Drug Resistant; **WHO:** World Health Organization.

SUMMARY

This prospective observational study aimed to investigate the susceptibility and resistance patterns of priority 1 critical gram-negative bacteria-*Pseudomonas aeruginosa, Klebsiella pneumoniae, Acinetobacter baumannii,* and *Escherichia coli*-to various antibiotics and to evaluate the efficacy of these antibiotics. Conducted over nine months, the study utilized an antibiogram approach to assess antibiotic susceptibility among 201 participants. Statistical analysis was conducted using JASP software. The results highlighted *Escherichia coli* as the predominant gram-negative pathogen, posing significant challenges due to its increasing resistance patterns. Among the antibiotics tested, Cefoperazone+sulbactam and piperacillin+tazobactam exhibited the highest susceptibility rates, indicating their effectiveness against these bacteria. Conversely, carbapenems (meropenem, imipenem), ampicillin and ertapenem showed the highest levels of resistance.

Furthermore, the study employed Student's paired T-test to analyze biomarkers including C-Reactive Protein (CRP), Procalcitonin and Erythrocyte Sedimentation Rate (ESR), revealing statistically significant findings that underscored the clinical implications of antibiotic resistance.

In conclusion, this study underscores the escalating challenge posed by Multidrug-Resistant organisms (MDR), particularly among critical gram-negative bacteria. It emphasizes the imperative of judicious antibiotic use to optimize infection control measures and enhance patient outcomes within healthcare settings. These findings contribute to the broader understanding of antibiotic stewardship and underscore the necessity for continued surveillance and adaptation in combating antibiotic resistance.

REFERENCES

1. Umemura T, Kato H, Hagihara M, Hirai J, Yamagishi Y, Mikamo H. Efficacy of combination therapies for the treatment of multi-drug resistant Gram-negative bacterial infections based on meta-analyses. Antibiotics (Basel) [Internet]. 2022 cited 2024;11(4):524. Available from: http://dx.doi.org/10.3390/antibiotics11040524
2. Goldstein RC, Husk G, Jodlowski T, Mildvan D, Perlman DC, Ruhe JJ. Fluoroquinolone- and ceftriaxone-based therapy of community-acquired *pneumonia* in hospitalized patients: The risk of subsequent isolation of multidrug-resistant organisms. Am J Infect Control [Internet]. 2014 cited 2024;42(5):539-41. Available from: https://pubmed.ncbi.nlm.nih.gov/24773792/
3. Boucher HW, Talbot GH, Bradley JS, Edwards JE, Gilbert D, Rice LB, *et al.* Bad bugs, no drugs: No ESKAPE! An update from the infectious diseases society of America. Clin Infect Dis [Internet]. 2009 cited 2024;48(1):1-12. Available from: https://pubmed.ncbi.nlm.nih.gov/19035777/
4. Matlock A, Garcia JA, Moussavi K, Long B, Liang SY-T. Advances in novel antibiotics to treat multidrug-resistant gram-negative bacterial infections. Intern Emerg Med [Internet]. 2021 cited 2024;16(8):2231-41. Available from: https://pubmed.ncbi.nlm.nih.gov/33956311/
5. Magiorakos A-P, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, *et al.* Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect [Internet]. 2012 [cited 2024;18(3):268-81. Available from: https://pubmed.ncbi.nlm.nih.gov/21793988/
6. Wright H, Bonomo RA, Paterson DL. New agents for the treatment of infections with Gram-negative bacteria: restoring the miracle or false dawn? Clin Microbiol Infect [Internet]. 2017 cited 2024;23(10):704-12. Available from: https://pubmed.ncbi.nlm.nih.gov/28893690/
7. Ortega B, Groeneveld ABJ, Schultsz C. Endemic Multidrug-Resistant *Pseudomonas aeruginosa* in Critically Ill Patients. Infect Control [Internet]. 2004 cited 2024;25(10):825-31. Available from: https://pubmed.ncbi.nlm.nih.gov/15518023/
8. Farooq L, Memon Z, Ismail MO, Sadiq S. Frequency and antibiogram of multi-drug resistant *Pseudomonas aeruginosa* in a Tertiary Care Hospital of Pakistan: MDR *Pseudomonas aeruginosa*. Pak J Med Sci Q [Internet]. 2019 [cited 2024 Aug 30];35(6): 1622. Available from: http://dx.doi.org/10.12669/pjms.35.6.930
9. Li J, Nation RL, Owen RJ, Wong S, Spelman D, Franklin C. Antibiograms of multidrug-resistant clinical *Acinetobacter baumannii*: Promising therapeutic options for treatment of infection with colistin-resistant strains. Clin Infect Dis [Internet]. 2007 cited 2024;45(5):594-8. Available from: https://pubmed.ncbi.nlm.nih.gov/17682994/
10. Cerceo E, Deitelzweig SB, Sherman BM, Amin AN. Multidrug-resistant gram-negative bacterial infections in the hospital setting: Overview, implications for clinical practice and emerging treatment options. Microb Drug Resist [Internet]. 2016 cited 2024;22(5):412-31. Available from: https://pubmed.ncbi.nlm.nih.gov/26866778/Researchgate.net. [cited 2024 Aug 30]. Available from: https://www.researchgate.net/publication/274639952_INCREASE_IN_ANTIBIOTIC_RESISTANCE_ARE_BACTERIA_GROWING_WITH_PAN_RESISTANCE
11. Pawar SK, Shinde RV, Patil HV, Patil SR, Karande GS, Mohite ST. Multidrug resistant gram-negative bacilli in clinical isolates in a tertiary care hospital [Internet]. Ijhsr.org. [cited 2024 Aug 30]. Available from: https://www.ijhsr.org/IJHSR_Vol.4_Issue.9_Sep2014/12.pdf
12. Alnajjar MS, Aldeyab MA, Scott MG, Kearney MP, Fleming G, Glimore F, *et al.* Influence of primary care antibiotic prescribing on incidence rates of multidrug-resistant Gram-negative bacteria in hospitalised patients. Infection. 2019;47(5):781-791. doi: 10.1007/s15010-019-01305-6. Epub 2019 May 7. PMID: 31065996.
13. Jayaprada R, Chaudhury A, Venkataramana B, Shobha Rani A. Pan-resistance among gram-negative clinical isolates at a tertiary care hospital in south India [Internet]. Nic.in. [cited 2024 Aug 30]. Available from: https://svimstpt.ap.nic.in/jcsr/jul-sep%2012_files/jul-sep%202012/oa2.pdf

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